

Title: RENILLA REINFORMIS FLUORESCENT PROTEINS,
NUCLEIC ACIDS ENCODING THE FLUORESCENT
PROTEINS AND THE USE THEREOF IN
DIAGNOSTICS, HIGH THROUGHPUT SCREENING
AND NOVELTY ITEMS.

Applicant: Bryan et al. Our Docket No.: 24729-0128
Serial No. 09/808,898 Filed: March 15, 2001

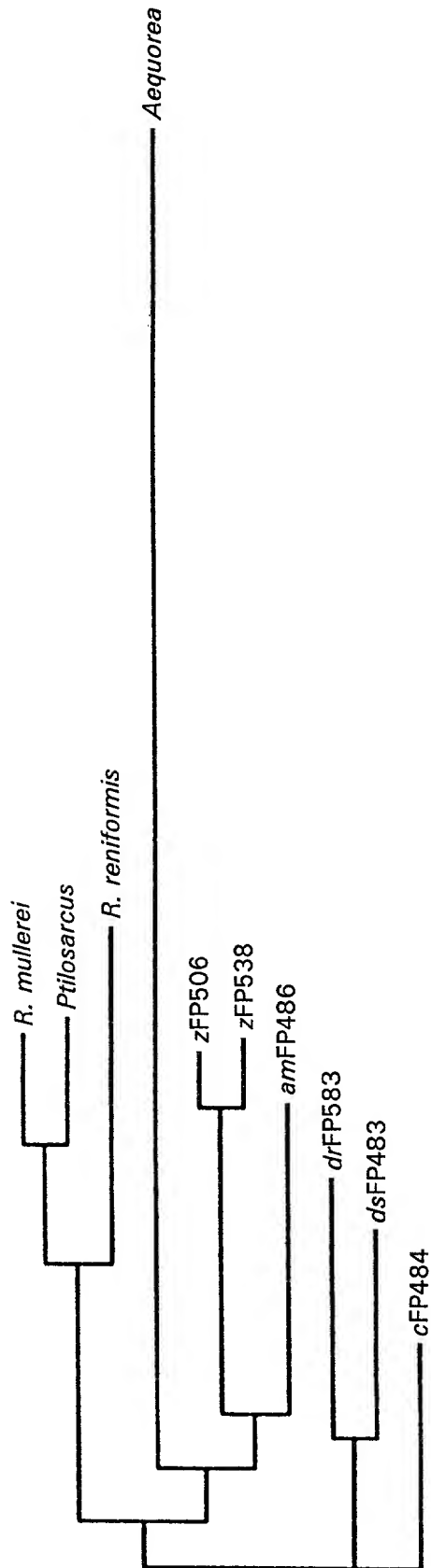


FIG. 1

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FIG. 2A

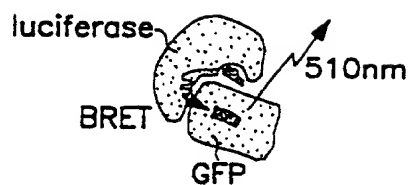


FIG. 2C

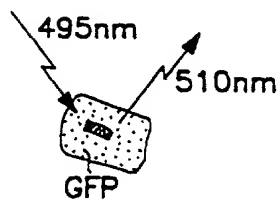


FIG. 2B

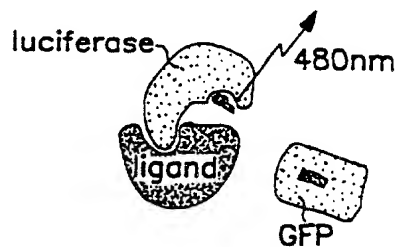
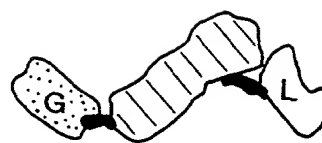


FIG. 2D

BRET Sensor Architectures

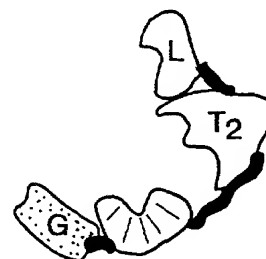
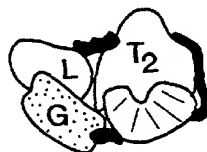
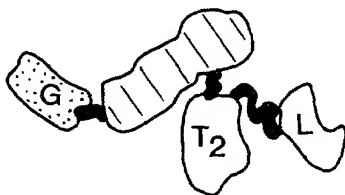
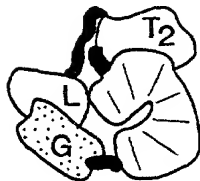
15°

37°



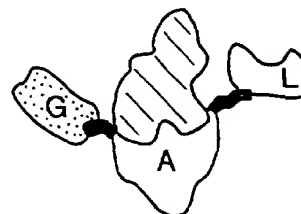
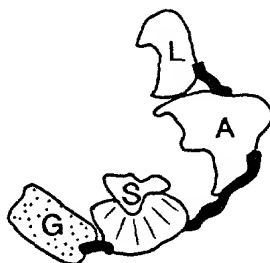
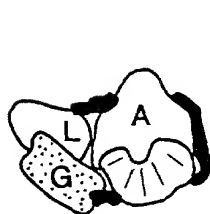
optimized energy transfer module

simple conformational change



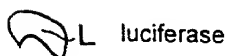
complex conformational change

association/dissociation



small molecule interference

large molecule interference



BRET sensors are depicted for permissive and non-permissive binding states of the target molecules. Binding may be modulated by varying temperature or ionic strength.

FIG. 3

Utilization of advantageous GFP surfaces with
 substituted fluorophores

	60	*	80	
RM-GFP	:	GAPLPFAFDIVSPAFAQYGNRTFTKYPNDIS--	:	83
Pt-GFP	:	GGPLPFAFDIVSIAFAQYGNRTFTKYPDDIA--	:	83
RR-GFP	:	GAPLPFAFDIVSVAFSYGNRAYTGYPEEIS--	:	80
cFP484	:	GAPLPFSYDILSNAFAQYGNRALTKYPDDIA--	:	83
drFP583	:	GGPLPFAWDILSPQFQYGSKVYVKHPADIP--	:	80
asFP595	:	GGPLPFAFHILSTSCMYGSKTFIKYVSGIP--	:	77
dsFP483	:	GGPLPFGWHILCPQFQYGNKAFVHHDPDNIH--	:	80
amFP486	:	GGPLAFSFDILSTVFKYGNRCFTAYPTSMP--	:	82
zFP506	:	GGPLPFAEDILSAAFNYGNRVFTEYPQDIV--	:	80
zFP538	:	GGPLPFSSEDILSAGFKYGDRIFTEYPQDIV--	:	80
=====				

FIG. 4

R_reniform	20	40	60	63
R_mullerei	20	40	60	66
Ptilosarcu	20	40	60	66
drFP583	20	40	60	63
	80	100	120	
R_reniform	80	100	120	129
R_mullerei	80	100	120	132
Ptilosarcu	80	100	120	132
drFP583	80	100	120	129
	140	160	180	
R_reniform	140	160	180	195
R_mullerei	140	160	180	198
Ptilosarcu	140	160	180	198
drFP583	140	160	180	195
	200	220	240	
R_reniform	200	220	240	233
R_mullerei	200	220	240	238
Ptilosarcu	200	220	240	238
drFP583	200	220	240	226

FIG. 5

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	*	20	*	40	*	60	80																																																																								
Aequorea	---	MSKGEELTG	VVP	IL	VEL	DG	VN	G	H	F	S	V	S	G	E	G	E	G	D	A	T	Y	G	K	L	T	L	K	F	C	T	T	---	G	K	L	P	F	P	V	P	T	L	V	T	F	S	Y	G	V	C	F	S	R	P	D	H	M	K	:	79																		
R mullerei	---	MSKQILKNT	CL	Q	E	V	M	S	K	V	N	L	E	G	I	V	N	N	H	V	F	T	M	E	G	G	K	N	I	L	F	G	N	L	V	Q	I	R	V	T	---	G	A	P	L	P	F	A	D	I	V	S	P	A	F	Y	G	N	R	T	F	T	K	P	N	D	I	---	82										
Ptilosarcu	---	MNRNLKNT	GL	K	E	I	M	S	A	K	S	A	V	E	G	I	V	N	N	H	V	F	T	M	E	G	G	K	N	I	L	F	G	N	L	V	Q	I	R	V	T	---	G	G	P	L	P	F	A	D	I	V	S	L	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	82									
R reniform	---	MDLAKLGL	K	E	V	M	P	T	K	I	N	L	E	G	I	V	N	N	H	V	F	T	M	E	G	G	K	N	I	L	F	G	N	L	V	Q	I	R	V	T	---	G	A	P	L	P	F	A	D	I	V	S	L	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	79										
drFP583	---	MRSSKNVI	K	E	F	M	R	F	K	V	R	M	E	G	I	V	N	N	H	V	F	T	M	E	G	G	E	G	R	P	Y	E	G	H	N	T	V	K	L	V	T	---	G	G	P	L	P	F	A	D	I	V	S	P	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	79									
drFP593	---	MSCSNVIK	E	F	M	R	F	K	V	R	M	E	G	I	V	N	N	H	V	F	T	M	E	G	G	E	G	R	P	Y	E	G	H	N	T	V	K	L	V	T	---	G	G	P	L	P	F	A	D	I	V	S	P	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	79										
dsFP483	---	MSCSKVIK	E	M	L	I	D	L	H	E	G	I	V	N	N	H	V	F	T	M	E	G	G	E	G	R	P	Y	E	G	H	N	T	V	K	L	V	T	---	G	G	P	L	P	F	A	D	I	V	S	P	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	79												
cFP484	---	KALTMTG	V	I	K	P	D	M	K	I	K	L	M	E	G	N	V	N	H	V	F	T	M	E	G	E	G	K	P	Y	E	G	H	N	T	V	K	L	V	T	---	G	G	P	L	P	F	A	D	I	V	S	P	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	82										
asFP595	---	MASFLK	T	M	P	F	K	T	I	E	G	I	V	N	N	H	V	F	T	M	E	G	G	E	G	K	P	Y	E	G	H	N	T	V	K	L	V	T	---	G	G	P	L	P	F	A	D	I	V	S	P	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	76												
amFP486	---	MALSNK	F	I	G	D	M	K	T	Y	H	M	D	G	V	N	H	V	F	T	M	E	G	G	K	P	Y	E	G	H	N	T	V	K	L	V	T	---	G	G	P	L	P	F	A	D	I	V	S	P	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	81													
zFP538	---	MAHSKH	G	L	K	E	E	M	T	K	Y	H	M	E	G	V	N	H	V	F	T	M	E	G	G	K	P	Y	E	G	H	N	T	V	K	L	V	T	---	G	G	P	L	P	F	A	D	I	V	S	P	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	79												
zFP506	---	MAQSKH	G	L	T	K	E	M	T	K	Y	H	M	E	G	V	N	H	V	F	T	M	E	G	G	K	P	Y	E	G	H	N	T	V	K	L	V	T	---	G	G	P	L	P	F	A	D	I	V	S	P	A	F	Y	G	N	R	T	F	T	K	P	D	D	I	---	79												
Aequorea	---	RHDFK	S	A	M	P	E	G	Y	V	Q	E	R	T	I	F	F	K	D	C	N	V	K	T	R	A	E	V	K	F	E	G	---	D	T	L	V	N	R	I	E	L	K	I	G	I	D	F	K	E	D	G	N	I	L	G	H	K	L	E	Y	N	S	H	N	I	T	M	A	D	K	Q	K	N	G	I	K	---	162
R mullerei	---	SDYFI	Q	S	F	P	A	G	F	M	Y	E	R	T	L	R	Y	E	D	G	L	V	E	R	S	D	I	N	L	E	---	D	K	F	Y	H	V	E	R	K	S	N	F	P	D	D	G	P	V	M	Q	K	T	I	---	L	G	I	E	P	S	F	E	A	M	Y	---	161											
Ptilosarcu	---	ADYF	Q	S	F	P	A	G	F	F	E	R	N	L	R	F	E	D	G	A	I	V	D	I	R	S	D	I	S	L	E	---	D	K	F	Y	H	V	E	R	K	S	N	F	P	D	D	G	P	V	M	Q	K	A	I	---	L	G	M	E	P	S	F	E	V	W	Y	---	161										
R reniform	---	ADYF	Q	S	F	P	E	G	F	T	E	R	N	L	R	Y	Q	D	G	I	A	I	V	D	I	S	L	E	D	---	G	K	F	I	V	N	D	F	K	A	I	R	M	G	P	V	M	Q	D	I	---	L	G	M	E	P	S	F	E	V	W	Y	---	158															
drFP583	---	PDYK	L	S	F	P	E	G	F	K	W	E	R	V	N	F	E	D	G	V	N	I	T	Q	S	S	L	Q	---	G	G	F	I	Y	K	K	E	I	G	N	F	S	D	G	P	V	M	Q	K	T	---	M	G	E	A	S	T	E	R	L	Y	---	158																
drFP593	---	PDYK	L	S	F	P	E	G	F	K	W	E	R	V	N	F	E	D	G	V	N	I	T	Q	S	S	L	Q	---	G	G	F	I	Y	K	K	E	I	G	N	F	S	D	G	P	V	M	Q	R	R	T	---	R	G	E	A	S	S	E	R	L	Y	---	158															
dsFP483	---	HDYK	L	S	F	P	E	G	F	T	M	E	R	S	M	H	F	E	D	G	L	C	T	I	N	I	S	L	T	---	N	C	F	I	Y	E	K	I	G	N	F	S	D	G	P	V	M	Q	R	R	T	---	R	G	E	A	S	S	E	R	L	Y	---	158															
cFP484	---	ADYF	Q	S	F	P	E	G	F	T	M	E	R	S	M	H	F	E	D	G	L	C	T	I	N	I	S	L	T	---	N	C	F	I	Y	E	K	I	G	N	F	S	D	G	P	V	M	Q	R	R	T	---	R	G	E	A	S	S	E	R	L	Y	---	158															
asFP595	---	PDYF	Q	S	F	P	E	G	F	T	M	E	R	S	M	H	F	E	D	G	L	C	T	I	N	I	S	L	T	---	N	C	F	I	Y	E	K	I	G	N	F	S	D	G	P	V	M	Q	R	R	T	---	R	G	E	A	S	S	E	R	L	Y	---	158															
amFP486	---	PDYF	Q	S	F	P	E	G	F	T	M	E	R	S	M	H	F	E	D	G	L	C	T	I	N	I	S	L	T	---	N	C	F	I	Y	E	K	I	G	N	F	S	D	G	P	V	M	Q	R	R	T	---	R	G	E	A	S	S	E	R	L	Y	---	155															
zFP538	---	PDYF	Q	A	F	P	D	C	M	S	Y	E	R	T	I	T	E	D	G	G	F	A	H	Q	D	T	S	L	D	---	D	C	L	V	K	K	I	L	N	N	F	H	A	D	G	P	V	M	Q	N	K	A	---	G	R	W	E	P	A	T	E	I	V	Y	---	160													
zFP506	---	VDYF	K	N	S	C	P	A	G	Y	T	M	G	R	S	F	L	E	E	D	G	A	V	C	I	N	V	D	I	T	S	V	K	E	N	C	I	Y	H	K	S	I	F	N	G	N	F	P	A	D	G	P	V	M	K	M	T	---	T	N	W	E	A	S	C	E	K	I	M	P	V	K	Q	I	L	K	---	162	
Aequorea	---	VNF	K	I	R	N	I	E	D	G	S	V	Q	L	A	D	H	Y	Q	N	T	P	I	G	---	D	G	P	V	L	L	P	N	I	T	S	Q	A	L	S	K	D	P	N	E	K	R	D	H	M	V	L	E	F	V	T	A	A	G	I	T	H	G	M	D	E	L	Y	K	---	238								
R mullerei	---	CEVIL	I	V	K	L	S	G	N	V	S	C	H	M	K	I	L	M	S	K	G	---	V	V	K	E	F	S	Y	H	I	Q	H	R	L	E	K	T	Y	V	E	D	G	F	---	V	E	Q	H	E	T	A	L	A	Q	M	T	S	I	G	K	P	L	S	L	H	E	W	---	238									
Ptilosarcu	---	CEVD	I	V	K	L	S	G	N	V	S	C	H	M	K	I	L	M	S	K	G	---	G	V	K	E	F	P	Y	H	I	Q	H	R	L	E	K	T	Y	V	E	E	G	S	F	---	V	E	Q	H	E	T	A	L	A	Q	L	T	I	I	G	K	P	L	S	L	H	E	W	---	238								
R reniform	---	CECII	A	F	K	L	Q	T	K	T	F	T	H	M	R	T	V	K	S	K	---	P	V	E	T	M	P	I	X	H	I	Q	H	R	L	V	K	T	N	V	D	T	A	S	G	---	Y	V	Q	H	E	T	A	L	A	A	H	S	T	I	K	K	I	E	G	S	L	P	---	233									
drFP583	---	CEI	H	K	A	L	K	D	G	G	H	L	V	E	F	K	S	I	T	M	A	K	---	A	P	V	Q	L	P	G	Y	N	V	D	S	K	L	D	I	T	S	H	N	E	D	Y	T	---	I	V	E	Q	Y	E	R	T	P	G	R	H	H	I	F	L	---	226													
drFP593	---	GDII	M	A	L	R	E	G	G	H	V	L	V	E	F	K	S	I	T	M	A	K	---	P	S	V	Q	L	P	G	Y	N	V	D	S	K	L	D	M	T	S	H	N	E	D	Y	T	---	V	V	E	Q	Y	E	K	T	Q	G	R	H	H	I	F	L	---	230													
dsFP483	---	GDII	H	A	L	T	V	E	G	G	H	V	A	D	I	K	T	V	R	A	K	---	A	A	K	M	P	G	Y	H	V	D	T	K	L	V	I	W	N	N	D	K	E	F	M	---	K	V	E	E	H	E	T	A	V	A	R	H	H	I	F	Y	E	P	K	K	D	---	232										
cFP484	---	GDII	S	H	L	L	E	G	G	H	V	R	C	F	K	S	I	T	M	A	K	---	K	V	V	K	L	P	D	Y	H	V	D	H	R	I	E	I	L	N	H	D	K	D	Y	N	---	K	V	T	L	Y	E	N	A	V	A	R	Y	S	I	L	L	P	S	Q	A	---	231										
asFP595	---	QCS	I	M	A	L	K	C	P	G	G	R	H	L	T	C	H	L	H	T	I	R	S	K	P	A	S	A	L	K	M	P	G	F	E	D	H	R	I	E	I	M	E	E	V	E	K	G	---	C	Y	K	Q	Y	E	A	V	A	A	C	R	Y	C	D	A	A	P	S	K	L	G	H	N	---	232				
amFP																																																																															